AMENDMENTS TO THE DRAWINGS

None.

REMARKS

The above-reference Office Action has been carefully reviewed and reconsideration thereof is respectfully requested.

The claims are objected to as not complying with 37 CFR 1.173(b). It is believed that the above amendment fully complies with 37 CFR 1.173(b).

Claims 1-4 have been rejected under 35 USC 112, second paragraph, as being indefinite. It is believed that the amendments to Claims 1 and 4 fully overcome this ground of rejection.

Claims 1-4 have been rejected under the judicially created doctrine of obviousness-type double patenting over Claims 1-4 of US Patent No. 5,962,478. Applicant respectively traverses this ground of rejection.

In the language of the '478 patent pointed to by the Examiner refers, in part, to a condition "caused" by neoplastic disease. In such causation, the neoplastic disease "causes" the cells affected by the neoplastic disease to release TNF-α. Column 20 of the patent should read down to line 7 rather than simply down to line 4. This includes the other clinical situations where the disease or disorder "causes" the release of excessive quantities of TNF-α from the adjacent tissues that are being damaged that otherwise were normal, (except they were damaged by the infection or by the release of substances from neoplastic cells which are toxic to the adjacent normal cells, causing the normal cells to release TNF-α).

There is nothing cited in the patent that suggests that neoplastic disease itself can be treated by pirfenidone or the other pyridones cited. The only thing cited for the pyridones in the patent is the inhibiting action of these compounds on the harmful effects of excessive levels of TNF-α cytokine on normal cells. TNF-α is not a growth factor cytokine that causes the proliferation or continued growth of neoplastic cells.

There is absolutely no suggestion, hint, or speculation anywhere in the patent that the cited pyridones would have an inhibitory effect on the proliferation or growth of cells found in tumors.

Referring to column 3, lines 12 through 18 of the cited patent, it is stated that "Although pathophysiological effects of TNF-α are generally limited to situations in which TNF-α tissue or serum levels are excessively high (such as occurs during gram-negative infections, allergic reactions, thermal burns, neoplasia and radiation or traumatic injury)..." This refers to the effect of the listed diseases on adjacent normal cells. These normal cells are being attacked by the cited diseases released to carry the excessive toxic quantities of TNF-α. Excessive amounts of TNF-α are prevented by pirfenidone and related compounds.

Since TNF-α is an important mediator of many reactive pathophysiologic states or diseases, inhibitors of TNF-α production can have utility in any pathophysiologic diseases in which abnormally high levels of TNF-α are present. The compounds of the invention described in the cited patent inhibit or block the (1) overproduction and release of TNF-α, and (2) pharmacologically inhibit or block the untoward toxic or lethal effects of high levels of TNF-α. Excessive TNF-α levels have been implicated in mediating or exacerbating a number of diseases including: rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis and other arthritic conditions; also general sepsis, gram-negative sepsis, septic-shock, endotoxic shock, toxic shock syndrome, adult respiratory distress syndrome (ARADS), cerebral malaria, chronic pulmonary inflammatory disease, silicosis, asbestosis, pulmonary sarcoidosis, bone resorption diseases, graft vs. host reactions, allograft rejections; also fever and myalgias due to bacterial or viral infections, such as influenza; cachexia secondary to acquired immune deficiency syndrome (AIDS), keloid formation, scar tissue formation, Crohn's disease, ulcerative colitis, or pyresis; a number of "autoimmune diseases" such as multiple sclerosis, autoimmune diabetes, and systemic lupus Erythematosus. (Tracey et al. *Nature*, 330: 662-664, 1987; Badger et al., *Circ*

Shock., 27:51-61, 1989 and Hinshaw et al., *Circ Shock.*, 30: 279-292, 1990; cachexia (Dezube et al. *Lancet*, 335 (8690: 662, 1990).

The term "prevention of the pathophysiologic effects of excessively high levels of TNF-α in tissues and organs" means the pharmacologic inhibition of the untoward, toxic or lethal effects of excessively high tissue levels of TNF-α. The pyridone compounds, by inhibiting or blocking the release, synthesis, as well as the pathophysiologic actions of excessive tissue levels of TNF-α in each of these circumstances, facilitates the resolution of the TNF-α induced tissue or organ damage. In the cited patent, we list the various types of commonly recognized tissues where TNF-α is a major factor in causing disease symptoms.

The listing includes the types or disorders including neoplastic disease that cause adjacent normal cells to be damaged and when they are damaged these normal cells produce large quantities of TNF-α. It is a large discharge of TNF-α by normal cells after attacks by adjacent infections, parasites and neoplastic cells. The attached normal cells thereby are induced to produce large quantities of TNF-α which in turn elicit more toxic effects on normal cells after these excessive levels of TNF-α.

Plain and simple, nowhere does the cited patent in any way suggest that the pirfenidone molecules or the other pyridone compounds inhibit growth of benign tumors or malignant tumors or leukemias to inhibit their cell proliferation or growth.

There is absolutely nothing in the cited patent which describes any anti-tumor action for any pyridones described. The only thing that is mentioned anywhere in the entire documents is the fact that certain tumors can cause a release of significant amounts of TNF-α from adjacent normal cells, and that this action could be inhibited by the pyridones.

Every every column, every paragraph, every sentence, and every single word in the cited patent has been reviewed and, and no single word or sentence that even suggests that tumor cells exposed to pirfenidone or any of the pyridone molecules inhibits the proliferation of growth of neoplastic cells or tissue can be found.

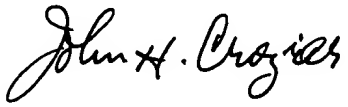
Quoting from the third full paragraph on page 3 of the Office Action "This is not persuasive. '478 discloses...that the action of blocking the release, synthesis, and pathophysiologic actions of excessive levels of TNF-α relates to the use of TNF-α inhibitors in treating neoplastic disease." Nowhere in the Examiner's cited paragraph is there a statement that pirfenidone can treat neoplastic disease. This is a gross error. There is nothing in the patent, not one word or sentence, that says that pyridone substances can be used to treat neoplastic disease as suggested by the Examiner.

In view of the above amendments and remarks, it is respectfully submitted that the claims in the application, Claims 1-4, are allowable and early action in that regard is respectfully requested.

Should the Examiner have any questions as to the allowability of the claims or any suggestions with respect thereto, the undersigned would be grateful for the privilege of a telephone conference with the Examiner.

Date: December 23, 2005.

Respectfully submitted,



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